

## LETTERS

**Long-term ACE Inhibitor Therapy in Diabetic Nephropathy: Potential Hazard?**

There is now an increasing long-term use of angiotensin-converting enzyme inhibitors (ACEIs) in the management of both incipient<sup>1</sup> and confirmed diabetic nephropathy<sup>2</sup> due to the established reno-protective effects of this class of drugs. However their side-effect profile has limited their universal usage, with concerns regarding the prevalence of cough (reported to be as high as 20%), first-dose hypotension (particularly with diuretic co-administration), precipitation of acute renal failure in the presence of renal artery stenosis and, on rare occasions, angioedema. Two recent cases of hyperkalaemia in association with ACEI therapy in diabetic nephropathy over several years have highlighted a potentially life-threatening but reversible side-effect of long-term therapy.

The first case is a 64-year-old woman with 8 years of known Type 2 diabetes mellitus (DM) complicated by diabetic retinopathy, nephropathy, and hypertension. Prior to commencement of ACEI therapy, serum potassium was 4.3 mmol L<sup>-1</sup>. After 6 years of continuous lisinopril (5 mg) treatment, serum potassium was consistently >6.0 mmol L<sup>-1</sup> with normal renal function. On ACEI withdrawal, serum potassium returned to pre-treatment level (4.7 mmol L<sup>-1</sup>) within 2 weeks. The second case of hyperkalaemia occurred in a 75-year-old woman with 14 years of Type 2 DM with confirmed diabetic retinopathy, nephropathy, renal impairment (urea 11.6 mmol L<sup>-1</sup>, creatinine 156 mmol L<sup>-1</sup> before ACEI treatment) and hypertension. After 14 years of ACEI therapy (enalapril 10 mg for 12 years which was replaced by perindopril 2 mg over the last 2 years), serum potassium was 6.0 mmol L<sup>-1</sup>, urea 22.2 mmol L<sup>-1</sup>, creatinine 292 mmol L<sup>-1</sup>. On withdrawal of ACEI, serum potassium fell to 5.6 mmol L<sup>-1</sup>, urea to 18.9 mmol L<sup>-1</sup>, and creatinine to 245 mmol L<sup>-1</sup>.

Both cases developed potentially hazardous hyperkalaemia following long-term ACEI therapy and occurred in the absence of other causes known to induce hyperkalaemia, such as increased potassium ingestion, treatment with potassium-sparing diuretics or non-steroidal anti-inflammatory drugs. The hyperkalaemia in the second case may have been secondary to the deterioration in renal function and compounded by ACEI, as both electrolyte and renal biochemistry improved on drug withdrawal. This suggests the

presence of co-existent renovascular disease. Diabetic patients may be at higher risk of developing hyperkalaemia due to the high prevalence of hyporeninaemic hypoaldosteronism,<sup>3</sup> direct effects of hyperglycaemia itself<sup>4</sup> or the presence of occult renovascular disease.

In a single recent survey in over 1700 diabetic outpatients, hyperkalaemia was found to be relatively common.<sup>5</sup> With the clear role of ACEI in the long-term management of diabetic nephropathy, therapy should be monitored by serum electrolytes not only before and shortly after initiation, but also as a routine in long-term follow-up.

**N.N. Chan, M.D. Feher\***

*Diabetes Unit, Clinical Pharmacology (ICSM)\*, Chelsea & Westminster Hospital, London SW10 9NH, UK*

**References**

1. The EUCLID study group. Randomised placebo-controlled trial of lisinopril in normotensive patients with insulin-dependent diabetes and normotensive patients with insulin-dependent diabetes and normoalbuminuria or microalbuminuria. *Lancet* 1997; **349**: 1787–1796.
2. Mogensen CE. Diabetic renal disease: the quest for normotension—and beyond. *Diabetic Med* 1995; **12**: 756–769.
3. Weidmann P, Reinhart R, Maxwell MH, Rowe P, Coburn JW, Massry SG. Syndrome of hyporeninemic hypoaldosteronism and hyperkalaemia in renal disease. *J Clin Endocrinol Metab* 1973; **36**: 965–977.
4. Goldfarb S, Cox M, Singer I, Goldberg M. Acute hyperkalaemia induced by hyperglycaemia: hormonal mechanisms. *Ann Int Med* 1976; **84**: 426–432.
5. Jarman PR, Kehely AM, Mather HM. Hyperkalaemia in diabetes: prevalence and associations. *Postgrad Med J* 1995; **71**: 551–552.

**Radio Emissions and Accutrend® Malfunction**

It has long been recognized that radio waves can induce malfunction of electronic devices. We have recently observed a situation where short-wave radio fields emitted by a radio station may have interfered with the performance of a portable, battery-operated reflectance photometer for determination of blood glucose (Accutrend®, Boehringer, Mannheim).

One of our patients with Type 2 diabetes

mellitus, starting intensified insulin therapy, converted to the use of a glucose meter (Accutrend®) that allowed more rapid measurements than her previously used device (Reflolux S®, Boehringer, Mannheim). She soon realized that at certain times the Accutrend® would produce values that differed substantially from those obtained using the Reflolux S® meter. The deviating Accutrend® results could be erroneously low or high, were not reproducible on a second measurement, and did not correspond to the colour of the test strip. When tested at our clinic, the meter gave satisfactory results both with test solutions and whole blood.

The patient lives only 500 m from a powerful short-wave radio station, which is operated at irregular intervals for international radio transmissions. She questioned whether radio fields emitted by the transmitter might be influencing performance of her meter. To test this hypothesis, she was instructed to compare normal Accutrend® measurements with measurements performed in a large metal box serving as a Faraday cage. On a subsequent occasion, a fasting blood glucose determination produced an unexpectedly low result (1.1 mmol L<sup>-1</sup>). The patient, who was asymptomatic, performed a second estimation with the meter placed in a metal box. The second determination showed a glucose concentration of 11.3 mmol L<sup>-1</sup>, in good agreement with a visual reading and a measurement obtained by Reflolux S®.

Boehringer, Mannheim states that the Accutrend® has been tested according to EC regulations and German laws regarding medical devices and their compatibility with electromagnetic fields. This case however suggests that short-wave radio fields may induce malfunction of portable blood glucose meters despite these precautions. In a specific situation individual meters may be affected differently.

**B. Mueller, P. Diem**

*Division of Endocrinology and Diabetes, Department of Internal Medicine, University of Bern, Inselspital, CH-3010 Bern, Switzerland*

**Radio Emissions and Accutrend Malfunction: Reply**

Thank you kindly for drawing our attention to this interesting case study. Boehringer Mannheim tests for all conceivable interference possibilities under everyday life circumstances, by complying with the regulations laid down by the EC. Due to the important nature of our devices, Boehringer Mannheim has internally and voluntarily raised these standards even